

## **Section II (Remarks)**

### **A. Regarding the Amendments**

As noted by the examiner at page 2 of the Office Action mailed September 11, 2009, the preliminary amendment mailed April 29, 2006 contained two claims numbered 15, presented sequentially. The examiner stated that “[t]here are two claims numbered 15. The claims need to be renumbered.” By the present response, the second claim numbered 15 has been amended to 16 and all subsequent claims have been renumbered, as indicated by the examiner “[f]or the examination purposes...” Therefore in both the published PCT application and the preliminary amendment, 46 total claims were presented. In the preliminary amendment claims 27-46 were cancelled. Accordingly, claims 1-26 were pending and under examination at the time of issuance of the September 11, 2009 Office Action, as noted by the examiner.

By the present Amendment, claims 1, 5 and 16-26 have been amended. No new matter within the meaning of 35 U.S.C. §132(a) has been introduced by the foregoing amendments. The amendments made herein are fully consistent with and supported by the originally-filed disclosure of this application.

Thus, upon entry of the amendments, claims 1-26 will remain pending and under examination.

### **B. Claim Objections**

At page 2 of the Office Action mailed September 11, 2009, the examiner objected to the claims as containing various informalities. The examiner’s attention is respectfully drawn to Section I above, providing amendments to the claims in response to the examiner’s objections. Specifically, the following amendments have been made:

- Claim 1 has been amended to recite 7 steps, labeled as steps (a)-(g). Step (f) was mistakenly added to the end of the text for step (e);
- Claim 5 has been amended to include the full text of that claim, as recited in the original application (filed as the published PCT application from which the present application claims priority). As amended, the claim is of proper dependent form;
- The second claim 15 has been renumbered to claim 16, as detailed in Section IIA above.

As amended, the claims no longer contain any subject matter objected to by the examiner. Withdrawal of the objections is respectfully requested.

**C. Rejection of Claims Under 35 U.S.C. §112**

In the September 11, 2009 Office Action at page 2, the examiner rejected claims 5, 16, 20, and 26 as failing to comply with the written description requirement of 35 U.S.C. §112, first paragraph.

Claim 5 was rejected with respect to the language "...wherein the electrochemical activator is selected n]-phosphonic acid, wherein n = 0-12." As set forth in detail above, a portion of the text of claim 5 was mistakenly omitted from the preliminary amendment mailed April 29, 2006. As amended, the claim recites in relevant part:

"...wherein the electrochemical activator is selected from the group consisting of poly(vinyl ferrocene), poly(vinyl ferrocene)-co-acrylamide, poly(vinyl ferrocene)-co-acrylic acid, poly(vinyl ferrocene)-co-acrylamido-(CH<sub>2</sub>)<sub>n</sub> sulfonic acid and poly(vinyl ferrocene)-co-acrylamido-(CH<sub>2</sub>)<sub>n</sub>-phosphonic acid, wherein n = 0-12."

As amended, the claim corresponds with the language of claim 5, as originally filed. As amended, claim 5 meets the written description requirement of 35 U.S.C. §112, first paragraph.

Additionally the examiner rejected claims 20 and 26 under 35 U.S.C. §112, second paragraph. Claim 20 was rejected for recitation of the limitation "the agent" in line 1 of the claim. However, claim 20 does not contain such a recitation. It is applicants' belief that the examiner intended to refer to renumbered claim 21, in view of the renumbered claims. The examiner's attention is respectfully drawn to amended claim 21, as set forth in Section I above. As amended, claim 21 no longer contains the term "the agent." The phrase "the electrochemical activator" has been alternately included. Support for this amendment can be found in the specification, for example in claim 3, in paragraph [0035] at page 9 or in paragraph [0060] at page 17 of the published PCT application. The rejection is therefore moot.

With respect to the rejection of claim 26, no basis of the rejection is provided. However, explanation of a previously unstated rejection of claim 16 is provided. It is applicants' belief that the rejection of claim 26 is a typographical error and that only rejection of claim 16 was

intended, as detailed in the last two lines of the rejection on page 3 of the Office Action mailed September 11, 2009.

Claim 16 was rejected as having insufficient antecedent basis for the limitation “capture molecule” in line 1 of the claim. The examiner’s attention is respectfully drawn to the language of amended claim 16, as set forth in Section I above. The claim has been amended to depend directly from claim 1, which recites capture molecules. As amended, the term “capture molecule” in claim 16 has antecedent basis in claim 1.

#### **D. Rejection of Claims Under 35 U.S.C. §102**

In the September 11, 2009 Office Action, claims 1, 6-19 and 23-26 were rejected under 35 U.S.C. §102(b) as being anticipated by Willner et al. (U.S. Patent No. 6,214,205). Applicants respectfully traverse the rejection.

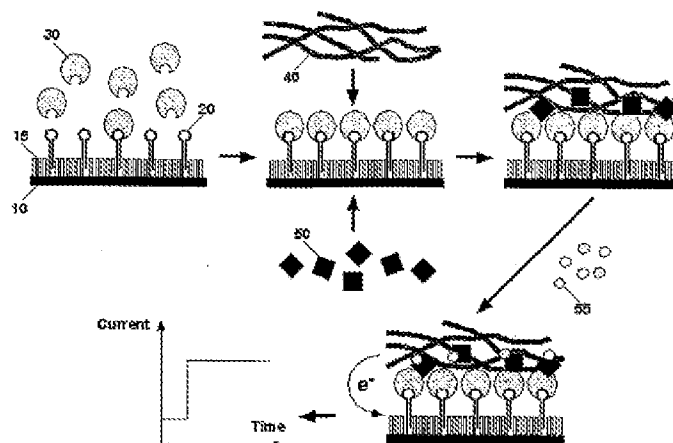
Anticipation of a claim requires the disclosure in a single prior art reference of each element of the claim under consideration. (Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987.)

Rejected claims 1, 18 and 26 are independent claims, from which rejected claims 6-17, 19, and 23-25 depend. The examiner alleged that Willner et al. teaches each step of the method of claim 1, the method of claim 18 and the biosensor of claim 26. Applicants respectfully disagree with the examiner’s characterization of the teachings of Willner et al with respect to the recited elements of the independent claims.

The examiner’s attention is respectfully drawn to each of claims 1 and 18, where formation of a conducting bilayer on the electrode is recited and to claim 26, where a biosensor containing such a bilayer is recited.

In claims 1 and 18, the capture molecule is immobilized at the surface of the electrode and forms a complex with the analyte, where the complex is a first layer on the electrode (step (c)). Next the electrode is contacted with an electrochemical activator, forming a second layer on the electrode (step (d)). Together these components form a conducting bilayer on the electrode. Formation of a bilayer is further illustrated in Figure 1A of applicant’s application, reproduced

below, where element 10 is the electrode, element 20 is the capture molecule, element 30 is the target analyte and element 40 is the electrochemical activator:



Independent claim 26 recites a biosensor containing such a bilayer. Each of the capture molecule, analyte and electrochemical activator is present in the bilayer on the electrode. Willner et al. does not describe a method of using such a conducting bilayer or a sensor containing such a bilayer.

In Willner et al., two competing reactions occur which can result in a change in the electrical current measured by the electrode. The measuring mechanism used in Willner et al. is illustrated, e.g., in Figures 3, 4 and 13 of Willner et al. As illustrated for example in Figure 3 of Willner et al., reproduced below, the electrode can have one member of a recognition pair (14 in Fig. 3A) and/or a first redox molecule (26 in Fig. 3A) bound directly thereto.

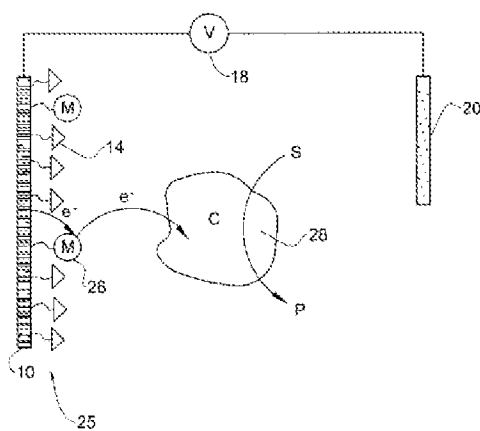


FIG. 3A

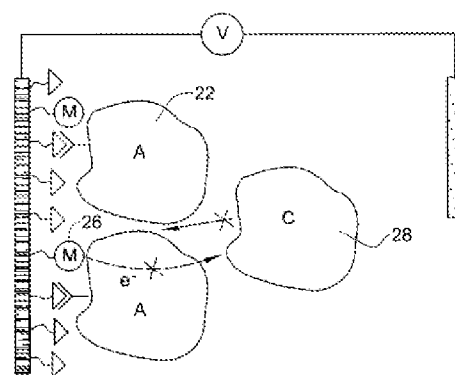
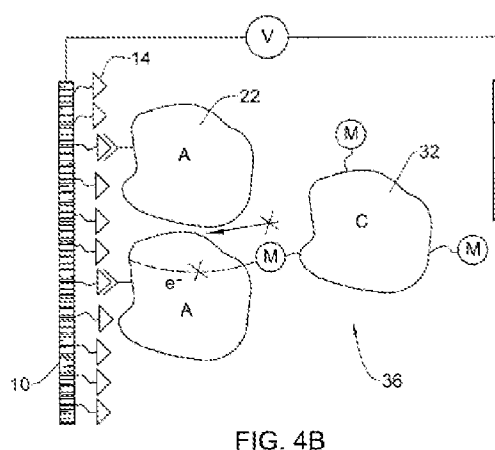
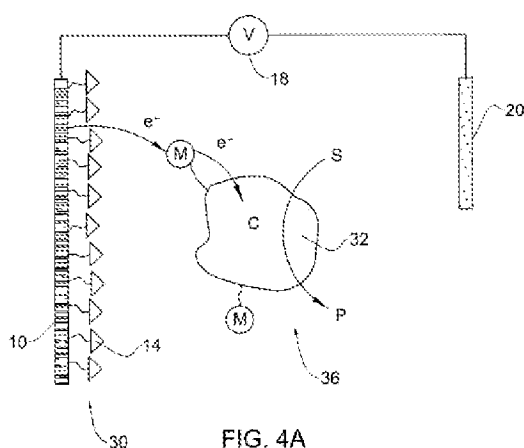


FIG. 3B

The recognition pair is capable of binding an analyte (22 in Fig. 3B) and the first redox molecule is capable of forming a complex with a second redox molecule (28 in Fig. 3). The complex formed by the first and second redox molecule results in a current flowing through the electrode (see, e.g. Figure 3A and col.4, line 61 to col.5, line 2, as well as col.5, lines 15 to 27). However, if a complex is formed between the analyte 22 and the immobilized binding partner 14, then no binding can occur between the redox molecules and no current flows through the electrode (see Figure 3B).

Figure 4 of Willner et al., reproduced below, illustrates another embodiment of that method (see also col.5, lines 29 to 37), in which the first redox molecule (M in a circle) is not bound to the surface of the electrode but forms a free floating complex 36 with the second redox molecule 32.



In the embodiment illustrated in Figure 4, if no analyte 22 binds to the immobilized binding partner 14 at the surface of the electrode, then the complex 36 (of first and second redox molecules) can reach the surface of the electrode and a current flows (Figure 4A). However, if the analyte is present and binds to the immobilized binding partner 14 at the surface of the electrode 10, no additional current can flow (Figure 4B) because the complex 36 is not able to bind the electrode.

Willner et al. describes a method where a current flows through the electrode only when the first and second redox molecules bind to form a layer in the absence of the analyte.

This aspect is also described in the general description of Willner et al., e.g. in col.5, lines 16 to 37. In this paragraph it is provided that when an analyte forms a complex with the binding

partner at the surface of the electrode, “there is a barrier for diffusion of the second redox molecule to the immobilized first redox molecule, yielding an impairment in the electron transfer...”

The examiner’s attention is further drawn to step (e) of claim 1 and step (d) of claim 18, as set forth in Section I above. Step (e) of claim 1 recites contacting the electrode with the bilayer formed thereon with “an agent capable of transferring electrons...” This further demonstrates that the agent capable of transferring electrons (enzyme or enzyme-conjugate, such as oxidoreductase) together with the electrochemical activator transfers electrons to or from the electrochemical activator and to or from the electrode in the presence of a first layer comprising the analyte bound to the capture molecule immobilized at the electrode surface (step (c)).

It is clear that in Willner et al. electron transfer does not depend on two different layers (bilayer) but only on the formation of one layer (first redox molecule and second redox molecule binding at the surface of the electrode), which will not form if conditions are favorable for an alternate layer (analyte and binding partner binding on the surface of the electrode). Willner et al. therefore teaches away from formation of an analyte-containing bilayer that is capable of electron flow.

Since Willner et al. do not describe a method as set forth in claim 1 or claim 18 or a biosensor as set forth in claim 26, Willner et al. do not anticipate the claimed invention. Claims 6-17 depend from claim 1 and claims 19 and 23-25 depend from claims 18 and therefore are patentable for the same reasons advanced above in support of the patentability of claims 1 and 18.

Accordingly, withdrawal of the rejection of claims 1, 6-19 and 23-26 under 35 U.S.C. § 102(b) as being anticipated by Willner et al. is respectfully requested.

#### **E. Rejection of Claims Under 35 U.S.C. §103**

In the September 11, 2009 Office Action, claims 2-4 and 9-21 were rejected under 35 U.S.C. §103(a) as being unpatentable over Willner et al. (U.S. Patent No. 6,214,205) as applied to claims 1, 6-18 and 22-25 and further in view of Zhiqiang et al. (Electrodeposition of Redox Polymer and Co-Electrodeposition of Enzymes by Coordinative Crosslinking, *Angew. Chem. Int. Ed.*, 2002, 41, 810-813).

Additionally, claim 5 was rejected under 35 U.S.C. §103(a) as being unpatentable over Willner et al. as applied to claims 1, 6-18 and 22-25 and further in view of Wefers et al. (U.S. Patent No. 5,132,181).

Each of the rejections set forth under 35 U.S.C. §103(a) relies on Willner et al. as a primary reference. As set forth in detail above, Willner et al. do not anticipate any of claims 1, 6-19 or 23-26. Rejected claims 2-5 and 9-21 depend, directly or indirectly from claim 1 or 18 and are therefore patentable for the same reasons advanced above in support of the patentability of claim 1. Neither of cited secondary references Zhiqiang et al. nor Wefers et al. remedies the deficiencies of Willner et al.

Based on the foregoing, Willner et al. in view of Zhiqiang et al. fail to provide any logical basis for a method comprising use of an electrode with an analyte-containing bilayer that is capable of electron flow formed thereon. The combination of Willner et al. and Zhiqiang et al. fails to render the method of claims 2-4 and 9-21 obvious. Accordingly, withdrawal of the rejection of claims 2-4 and 9-21 under 35 U.S.C. § 103(a) as being obvious over Willner et al. in view of Zhiqiang et al. is respectfully requested.

Additionally, Willner et al. in view of Wefers et al. fail to provide any logical basis for a method comprising use of an electrode with an analyte-containing bilayer that is capable of electron flow formed thereon. The combination of Willner et al. and Wefers et al. fails to render the method of claim 5 obvious. Accordingly, withdrawal of the rejection of claim 5 under 35 U.S.C. § 103 (a) as being obvious over Willner et al. in view of Wefers et al. is respectfully requested.

### **CONCLUSION**

Based on the foregoing, all of Applicants' pending claims 1-26 are patentably distinguished over the art, and in form and condition for allowance. The examiner is requested to favorably consider the foregoing, and to responsively issue a Notice of Allowance.

No fees are believed to be due for the filing of this paper. However, should any fees be required or an overpayment of fees made, please debit or credit our Deposit Account No. 08-3284, as necessary.

If any issues require further resolution, the examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss same.

Respectfully submitted,

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